

# Detection of Unstable Plaques in Patients with Carotid Stenosis using B-Mode Ultrasonography

E. KOBAYASHI, J. ONO\*, S. HIRAI, I. YAMAKAMI, N. SAEKI, A. YAMAURA

Department of Neurological Surgery, Chiba University School of Medicine

\* Department of Neurological Surgery, Chiba Cardiovascular Center

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## Summary

Distal embolism is a detrimental complication of stent placement for the carotid artery stenosis. To evaluate usefulness of B-mode ultrasonography (US) for the detection of unstable plaques in patients with carotid artery stenosis, we examined US in 46 arteries of 35 patients with carotid stenosis of >30%.

The echogenicity of 46 carotid plaques was hyperechoic in 20 plaques, hypoechoic in 15, and mixed-echoic in 11. The echogenicity of carotid plaques was correlated with severity of carotid stenosis, ipsilateral stroke or TIA, heart attack, and risk factors of systemic atherosclerosis. Hypoechoic plaques were associated with severe carotid stenosis and ipsilateral ischemic event. Mixed-echoic plaques had a high incidence of past history of heart attack. Hyperechoic plaques were less likely to associate with risk factors of systemic atherosclerosis.

We developed a new method of echodensity analysis. Using a computer software, echodensity values of seven plaque components were determined by comparing US findings and pathology of surgical specimens. The echodensity value was defined as a relative value to the arterial lumen.

The calcified part of plaques had the highest echodensity of  $6.24 \pm 0.86$  (mean  $\pm$  2 S.D.); fibrosis or hyarynoid degeneration of  $2.05 \pm 0.40$ ,

foamy histiocytes of  $1.47 \pm 0.05$ , necrosis of  $1.32 \pm 0.16$ , cholestelin clefts of  $1.28 \pm 0.13$ , intraplaque hemorrhage of  $1.02 \pm 0.09$ , and intraluminal thrombus of  $1.27 \pm 0.07$ . Constructed from the echodensity value, an echo-densitometry color mapping of the carotid plaque illustrated the exact location and extent of plaque component. B-mode US of carotid plaques represents clinical characteristics relating distal embolism and systemic atherosclerosis. A new method of echodensity analysis and echo-densitometry color mapping of the carotid plaque is useful to detect unstable plaques in patients with carotid stenosis.

## Introduction

Stent placement is a promising treatment option for the stenosis of cervical carotid arteries especially in high-risk patients<sup>1-3</sup>. Distal embolism during and after the stent placement is a detrimental complication of the procedure and even determines the outcome of patients. Although the currently available distal protective balloon system decreases the incidence of distal embolism<sup>4</sup>, complete protection of distal embolism is difficult. It is important to detect the unstable plaque that is likely to produce distal emboli by the stent placement.

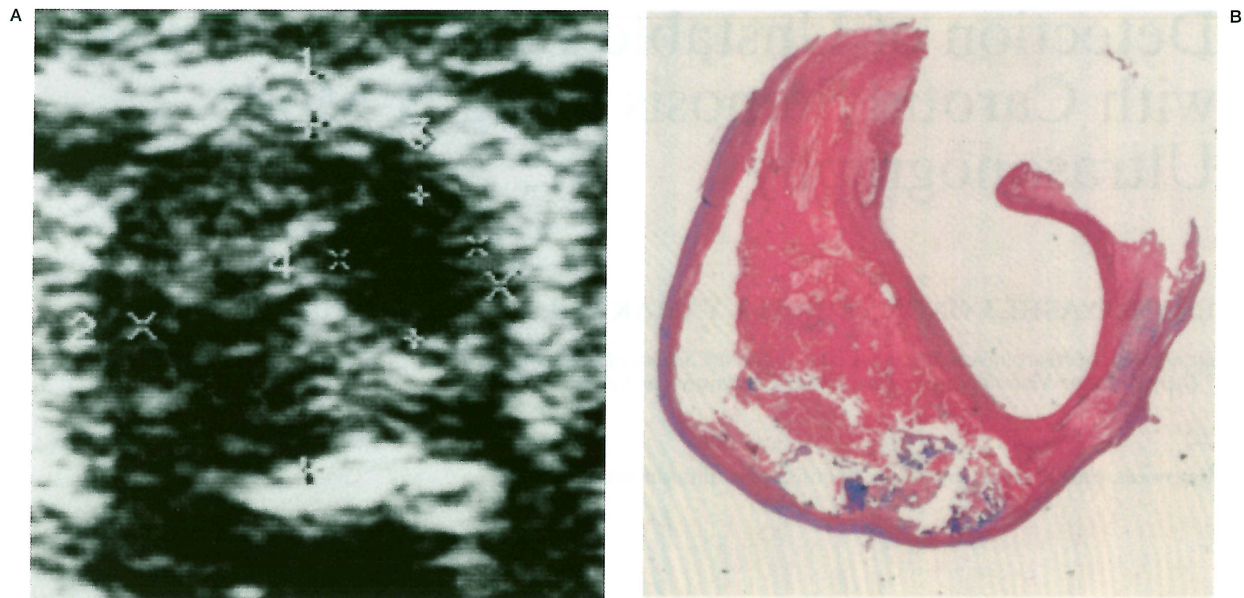


Figure 1 B-mode US scan (right) and corresponding surgical specimen (left). The echodensity of each plaque component is determined using computer software.

This study evaluated usefulness of B-mode ultrasonography (US) for detection of unstable plaques in patients with carotid stenosis and reported a new method of echodensity analysis and echo-densitometry color mapping of the carotid plaque.

### Material and Methods

From August 1998 to June 1999, carotid US was performed in 310 arteries to screen the carotid stenosis at Chiba University hospital. Color duplex ultrasonography was carried out by one experienced ultrasonographer (EK) using equipment Logic 500 MD TM (GE medical system) with a 7.5 MHz linear-array probe. This study comprises 46 carotid arteries of 35 patients with carotid stenosis of >30% on carotid US. The mean age of 35 patients was  $63.4 \pm 12.5$  years (23 males and 12 females). Hypertension (>160 mmHg in systolic blood pressure) was noted in 20 patients and diabetes (>5.5% in glycohemoglobin A1c) in 17 patients. Eleven patients had the bilateral carotid stenoses and 12 patients had the symptom corresponding to the carotid stenosis.

The echogenicity of the 46 carotid plaques were 20 plaques of hyperechoic, 15 of hypoechoic, and 11 of mixed-echoic. Relations of plaque echogenicity and clinical characteristics

were analyzed. Clinical characteristics analyzed were 1) stenosis rate of carotid artery, 2) ipsilateral stroke or TIA, 3) ipsilateral retinal ischemia, 4) ischemic heart disease, and 5) risk factors of systemic atherosclerosis (hypertension, diabetes, hyperlipidemia, ever smoking, obesity).

The stenosis rate was determined by a cross sectional US imaging at the maximal stenosis. Hyperlipidemia was defined as the triglycerides of >150 mg/dl or the total cholesterol of >220 mg/dl. Obesity was the body mass index of >28.6%. Smoking history was judged present if the patient had the habit at the time of examination. Heart attack and risk factors were analyzed regarding the patient.

In seven patients who underwent carotid endarterectomy (CEA), preoperative US findings of the plaque were compared with pathology of surgical specimens. Pathological examination of plaques revealed seven plaque components, i.e. calcification, fibrosis or hyaline degeneration, foamy histiocytes, necrosis, cholesterol clefts, intraplaque hemorrhage, and intraluminal thrombus.

Comparing US findings of each scanning slice with pathology of the corresponding surgical specimen using a computer software (Photoshop 5.0, Adobe), the echodensity value was determined for each of seven plaque



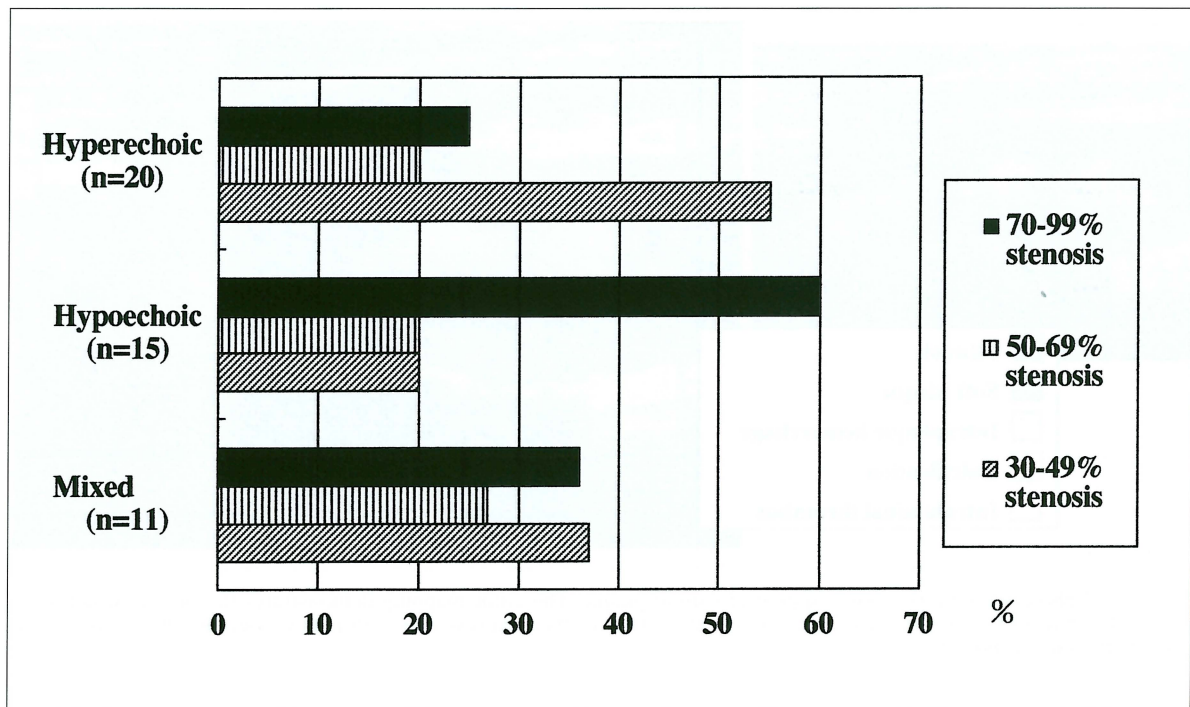


Figure 2 Relationship between plaque echogenicity and severity of carotid stenosis. Severe stenosis is common in hypoechoic lesions.

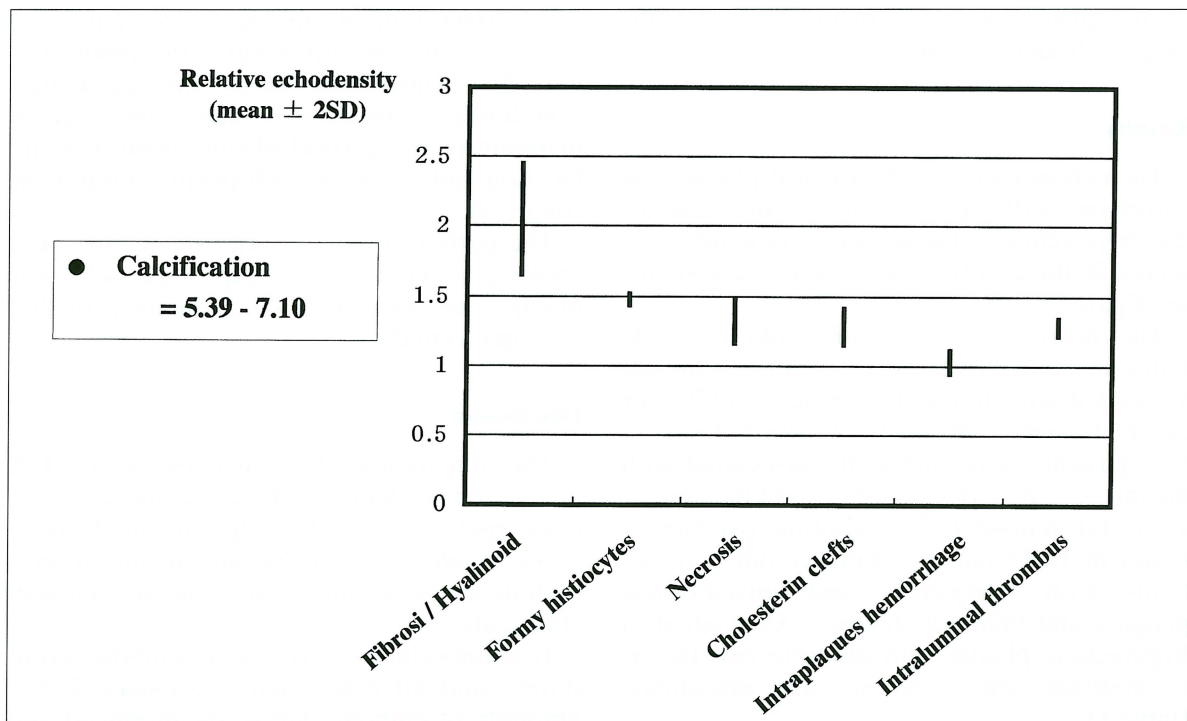


Figure 3 Echodensity value of plaque components. The echodensity value is defined as the relative value to the arterial lumen (mean value  $\pm$  2 S.D.).

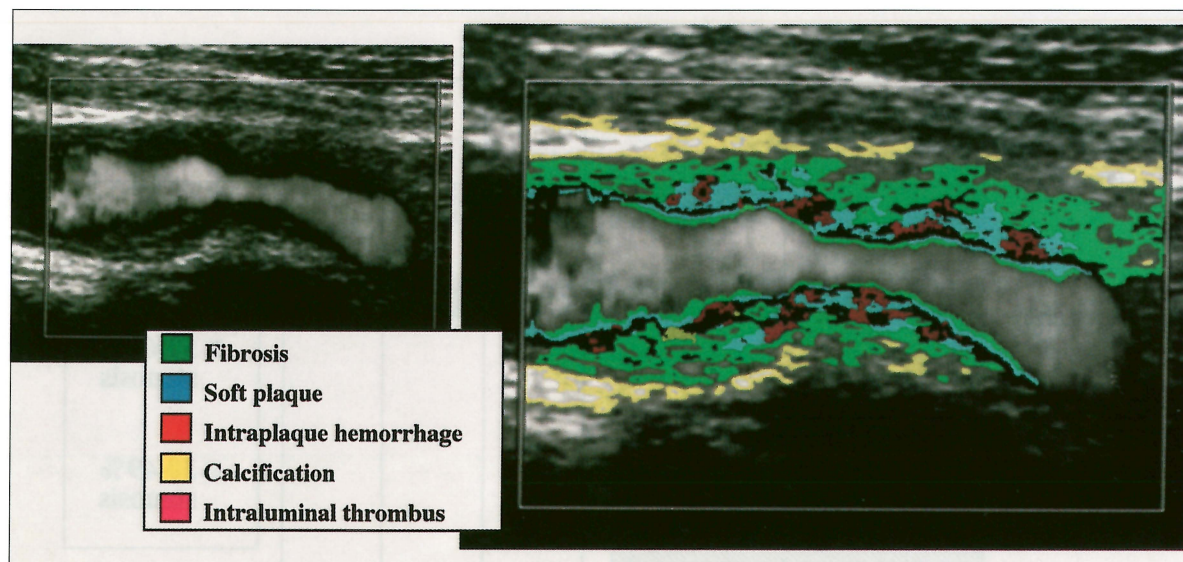


Figure 4 Echo-densitometry color mapping of carotid plaque. The color mapping demonstrates the precise structure of plaque. The part of foamy histiocytes, necrosis and cholestelin clefts is expressed as "soft plaque" because these components provide the same echodensity.

components: the echodensity value was defined as a relative value to the arterial lumen (figure 1).

An echo-densitometry color mapping of the carotid plaque was constructed from the obtained echodensity data.

## Results

The echogenicity of the carotid plaque was correlated with severity of carotid stenosis: the hypoechoic plaque was frequently observed in the carotid artery with severe stenosis (figure 2).

The history of ipsilateral stroke or TIA, found in 12/46 carotid arteries, was commonly associated with hypoechoic plaques (47%) or calcified plaques (50%). Heart attack, found in 8/35 patients, was commonly associated with the mixed-echoic plaque (38%) and the bilateral carotid stenoses (27%). Multiple risk factors, found in 18/35 patients, were common in patients with hypoechoic and mixed-echoic plaques, and bilateral stenoses. Association of hyperechoic plaque with multiple risk factors of systemic atherosclerosis was uncommon (table 1).

The echodensity value of seven plaque components was  $6.24 \pm 0.86$  (mean  $\pm$  2 S.D.) for the

calcified part of the plaque,  $2.05 \pm 0.40$  for the fibrosis or hyaline degeneration,  $1.47 \pm 0.05$  for the foamy histiocytes,  $1.32 \pm 0.16$  for the necrosis,  $1.28 \pm 0.13$  for the cholestelin clefts,  $1.02 \pm 0.09$  for the intraplaque hemorrhage, and  $1.27 \pm 0.07$  for the intraluminal thrombus (figure 3). Constructed from the calculated echodensity value, an echo-densitometry color mapping of the carotid plaque illustrated the location and extent of each plaque component (figure 4).

The parts of foamy histiocytes, necrosis and cholestelin clefts were expressed as "soft plaque" because these components provided the same echodensity.

## Discussion

The remarkable difference between CEA and stent placement is whether embolic source is extirpated or not. Although the stent placement expands the arterial lumen, the atheromatous plaque compressed in the arterial wall still exists.

It is important to prevent an embolic event during and after the stent placement. Large amounts of embolic debris are produced and migrate distal to cerebral circulation. Though the currently available distal protective balloon



Table 1 Echogenicity of carotid plaque and clinical characteristics

<b>1. Ipsilateral stroke or TIA</b>	
a) Hyperechoic lesions	2/20 arteries (10%)
Hypoechoic lesions	7/15 arteries (47%)
Mixed-echoic lesions	3/11 arteries (27%)
Total	12/46 arteries (24%)
b) Calcified lesions	5/10 arteries (50%)
Non-calcified lesions	7/36 arteries (19%)
Total	12/46 arteries (24%)
<b>2. Retinal ischemic event</b>	
Hyperechoic lesions	1/20 arteries (5%)
Hypoechoic lesions	2/15 arteries (13%)
Mixed-echoic lesions	2/11 arteries (18%)
Total	5/46 arteries (11%)
<b>3. Heart attack</b>	
Hyperechoic lesions	1/11 patients (9%)
Hypoechoic lesions	1/5 patients (20%)
Mixed-echoic lesions	3/8 patients (38%)
Total	8/35 patients (23%)
<i>Heart attack was observed in 3/11 (27%) patients with bilateral stenoses.</i>	
<b>4. Multiple risk factors</b>	
Hyperechoic lesions	1/11 patients (9%)
Hypoechoic lesions	3/5 patients (60%)
Mixed-echoic lesions	6/8 patients (75%)
Total	18/35 patients (51%)
<i>Multiple risk factors were present in 8/11 (73%) patients with bilateral stenoses.</i>	

system decreases distal embolism<sup>4</sup>, the complete protection is difficult.

Several authors have advocated the efficacy of US to extract unstable plaques that are likely to produce distal emboli by the stent placement<sup>5-9</sup>. A cohort study of 4886 individuals revealed high risk of incident stroke in the hypoechoic plaques<sup>10</sup>. Echolucent plaques are associated with elevated levels of fasting and postprandial triglycerides-rich lipoproteins<sup>6</sup>, and with intraplaque hemorrhage and risk of stroke<sup>11</sup>.

This study showed 1) hypoechoic plaques are associated with severe carotid stenosis and ipsilateral stroke or TIA, 2) hyperechoic plaques, probably an initial lesion with mild carotid stenosis, are not correlated with risk factors of atherosclerosis, 3) mixed-echoic plaques represent the systemic atherosclerosis rather than the carotid atherosclerosis.

It is not objective to classify the plaque echogenicity into hyperechoic, hypoechoic, and mixed-echoic. The carotid plaque is not homogenous and comprises several components different pathologically. The classification of the plaque echogenicity does not differentiate the plaque components.

To demonstrate the fine structure of the plaque, we developed a new method of echodensity analysis and echo-densitometry color mapping of the carotid plaque. Using a computer software, the echodensity value of seven plaque components is determined by comparing US findings with pathology of surgical specimens. Our results showed plaque components of foamy histiocytes, necrosis and cholesterol clefts provided the same echodensity, and were expressed as slight hypoechoic area on US.

These components represent the advanced atherosclerosis leading to rupture of the plaque. Intraluminal thrombus was identified as also somewhat hypoechoic on B-mode US and was detectable using densitometry mapping. We are now scheduling prospective study to select high-risk group for future stroke using this densitometry mapping.

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Eiichi Kobayashi, M.D.  
Department of Neurosurgery  
Chiba University School of Medicine  
1-8-1 Inohana  
Chuou-ku, Chiba 260-0856 Japan  
E-mail: papez@xa2.so-net.ne.jp